Surgical mortality at 30 days and complications leading to recraniotomy in 2630 consecutive craniotomies for intracranial tumors

[1]Benjamin Lassen, medical student, [1,2]Eirik Helseth MD, PhD, [2]Pål Rønning MD, [4]David Scheie MD, [5]Tom Børge Johannesen MD, PhD, [6]Jan Mæhlen MD, PhD, [1,2]Iver A. Langmoen MD, PhD, [3]Torstein R. Meling MD, Dr. phil.

[1]Faculty of Medicine, University of Oslo
[2]Department of Neurosurgery, Oslo University Hospital, Ullevål
[3]Department of Neurosurgery, Oslo University Hospital, Rikshospitalet
[4]Department of Pathology, Oslo University Hospital, Rikshospitalet
[5]The Norwegian Cancer Registry, Oslo, Norway,
[6]Department of Pathology, Oslo University Hospital, Ullevål

Corresponding author:

Torstein R. Meling, MD, Dr. phil.
Senior Consultant
Department of Neurosurgery
Oslo University Hospital, Rikshospitalet
N-0027 Oslo, Norway

Phone: +47 23074843
Fax: +47 23074310
E-mail: torsteinrmeling@mailcity.com
E-mail: torstein.meling@rikshospitalet.no

Abstract

Background:

In order to weigh the risks of surgery against the presumed advantages, it is important to have specific knowledge about complication rates.

Objective:

To study the surgical mortality and rate of reoperations for hematomas and infections after intracranial surgery for brain tumors in a large, contemporary, single-institution consecutive series.

Material & Methods:

All adult patients from a well-defined population of 2.7 mill. inhabitants who underwent craniotomies for intracranial tumors at Oslo University Hospital during 2003 to 2008 were included (n=2630). The patients were identified from our prospectively collected database and their charts studied retrospectively. Follow-up was 100%.

Results:

The overall surgical mortality, defined as death within 30 days of surgery, was 2.3% (n=60). The mortality rates for high- and low-grade gliomas, meningiomas, and metastases were 2.9%, 1.0%, 0.9%, and 4.5%, respectively. Age>60 (Odds ratio 1.84, $p<0.05$) and biopsy compared to resection (Odds ratio 4.67, $p<0.01$) were significantly positively associated with increased surgical mortality. Hematomas accounted for 35% of the surgical mortality. Postoperative hematomas needing evacuation occurred in 2.1% (n=54). Age >60 was significantly correlated to increased risk of postoperative hematomas (Odds ratio 2.43, $p<0.001$). A total of 39 patients (1.5%) were reoperated for postoperative infection. Meningiomas had an increased risk of infections compared to high grade gliomas (Odds ratio 4.61, $p<0.001$).

Conclusions:

Mortality within 30 days of surgery was 2.3%, with age >60 and biopsy vs. resection being the two factors significantly associated with increased mortality. Postoperative

hematomas caused about one third of the surgical mortality. The overall risk associated with surgery for intracranial tumors is low.

Running title:

Complications to surgery for brain tumors

Key words:

Craniotomy – Complications – Intracranial tumor – Postoperative hematoma – Postoperative infection – Surgical mortality – Survival

Introduction

According to The Central Brain Tumor Registry of the United States (CBTRUS), the incidence rate of all primary brain and central nervous system (CNS) tumors is 16.5 cases per 100,000 person–years (9.2 per 100,000 person–years for non–malignant tumors and 7.3 per 100,000 person–years for malignant tumors) [1]. The prevalence rate for all primary brain and central nervous system tumors was estimated to be 130.8 per 100,000 inhabitants [1]. Metastatic brain tumors are thought to have a higher incidence than primary brain tumors [2].

The cornerstone of brain tumor treatment is surgery. The objective of surgery is to remove as much tumor as possible, as well as to establish an exact tissue diagnosis. The possible benefits of tumor removal include symptom relief, improved quality of life, smaller tumor burden for other treatment modalities and improved survival [3-9].

However, craniotomies are not without inherent risks, be it surgical mortality [10, 11], postoperative hematomas [12, 13] or infection [14]. With respect to surgical mortality, the reported series are often of limited size [15] and based on a selected patient group [16]. Furthermore, to ascertain surgical deaths, either death before discharge (in-hospital mortality) or within 30 days of surgery is used, with the former missing more than 25% of surgery-related deaths and creates potential for bias across institutions (John D. Birkmeyer, personal communication). With respect to intracranial hematomas, the consequences are often devastating, with a mortality rate of 30% and a significant morbidity rate [17]. With respect to infections after neurosurgical procedures, these often present as meningitis, subdural empyema, or cerebral abscess. Although meningitis can often be treated with intravenous antibiotics, cases that involve a bone flap infection, subdural empyema, or cerebral abscess usually require a repeated operation.

In order to weigh the risks of surgery against the presumed advantages, it is important to have specific knowledge about the institution's complication rate. We therefore wanted to determine the 30 day surgical mortality rate as well as the rate of post-craniotomy hematomas and infections that required reoperation, reviewing our prospectively collected database of 2630 craniotomies for tumors performed between

2003 and 2008.

Materials and methods

Patients

The defined neurosurgical catchment area for Oslo University Hospital is the south and eastern health region of Norway. It has 2.7 million inhabitants (56% of the Norwegian population) and Oslo University Hospital treat approximately 99% of the neurosurgical tumor patients within this region (The Norwegian Cancer Registry, unpublished data). All patients ≥18 years who underwent craniotomy for an intracranial tumor at the two departments of Oslo University Hospital (Rikshospitalet and Ullevål) in the time period 2003 – 2008 were included in this study. Thus, this study can also serve as a population study in terms of incidence of craniotomies for particular tumor types in Norway. Patients who underwent stereotactic biopsy were not included.

The patients were identified from our prospectively collected database and their charts were studied retrospectively. The following data were recorded: sex, age, biopsy or resection, primary or secondary (repeated) surgery, histology, reoperation for postoperative hematoma, and reoperation for deep postoperative infection (infected bone flap, epidural abscess, subdural empyema or intracerebral abscess). Superficial wound infections that required simple wound revision were not included. Surgical mortality was defined as death within 30 days of surgery. Vital status (dead or alive) and time of death was obtained from the Norwegian Population Registry (Folkeregisteret) February 28th, 2009.

The charts of the patients who died within 30 days, or who were reoperated for hematoma or infection, were studied more thoroughly. The cause of death for those who died within 30 days was recorded as directly surgery-related (SR), i.e. hemorrhage or postoperative edema with subsequent herniation, or not surgery-related (NSR), i.e. either tumor progression-related, systemic complications, or other causes. The time from initial surgery to reoperation for hematoma or infection was recorded. The long-term outcome for those reoperated for hematoma or infection was determined, based on preoperative status, postoperative recovery, both after the original craniotomy and reoperation, and status at follow-up contacts with the hospital. The patient's condition at follow-up was compared with the patient's

expected disability had he not suffered such complications, thus giving an estimate of additional disability likely caused by the hematoma or infection. The following scale was used: no additional disability, minor additional disability, major additional disability, and death.

The major histological groups were used (Table 1), with low-frequency tumor types grouped as others. The gliomas were divided into two groups: High-grade gliomas (HGG), and low-grade gliomas (LGG). The HGG-group included glioblastoma multiforme (WHO grade IV), primitive neuroectodermal tumor (PNET) (WHO grade IV), anaplastic astrocytoma, anaplastic oligoastrocytoma, anaplastic oligodendroglioma, and anaplastic ependymoma (all WHO grade III). The LGG-group included all other astrocytic, oligodendroglial, ependymal tumors (WHO grade I and II), and also ganglioglioma (WHO grade I), DNET (WHO grade I), and choroid plexus tumors (WHO grade I and II).

Perioperative routines

A consultant anesthetist sees all our patients preoperatively. Elderly patients (>70 years) and patients on multiple medications are routinely also seen by consultant internist, to optimize the general medical condition and medications. Patients with a known heart condition are referred to cardiologist for cardiac ultrasound and ECG stress test. Patients with a past hematological history are referred to a consultant hematologist. Aspirin is stopped at least 10 days prior to surgery and when on anticoagulation, the INR should be below 1.5. All patients receive compressive stockings the day before surgery and keep them until fully mobilized. At initiation of surgery, a second-generation cephalosporin is administered intravenously and continued every 90 minutes until the case is completed or the maximum daily dose of 8 grams is reached. For long cases, erythromycin or a third-generation cephalosporin is started after the maximum daily dose of a second-generation cephalosporin is reached and continued until completion of the case. Postoperatively, the patients are observed in the recovery for 3-6 hours, whereafter they are transferred to a level 2 bed. After a craniotomy for a supratentorial tumor, the patients are generally observed for 24 hours. For infratentorial tumors, the length of observation is minimum 48 hours. Low-molecularweight heparin is given the first postoperative day. The

patients are mobilized either in the afternoon at the day of surgery or on the first postoperative day.

Ethics

The hospitals´ Data Protection Officials approved the study.

Statistics

Uni- and multivariate logistic regression was used to determine the impact of the different independent variables on 30 day mortality, postop hematoma and postop infection. The independent variables were binary except for histology where high grade glioma was used as the reference category against which all other histology classes were compared. The fit of the multivariate models were investigated and reported using Pseudo-R2 and the Hosmer-Lemeshow goodness-of-fit test. P-values less than 0.05 were considered significant. Stata v10.1 (Stata Corp, Austin, Tx) was used for all statistical analyses.

Results

Patient population

A total of 2630 consecutive craniotomies at the Oslo University Hospital in the time period 2003-2008 were included in this study (Table 1). The mean age at surgery was 56 years (range 18-89 years), with a male-to-female ratio of 1:1.06. Follow-up was 100%.

Incidence of craniotomies

First-time craniotomies with primary resection were performed in 2073 cases, 483 cases were reoperations with repeated resection, and 74 cases were open biopsies. Thus, the incidence of first-time craniotomy for a brain tumor was 12.8 /100 000 inhabitants per year and for a repeat resection 3.0 /100 000 inhabitants per year.

Surgical mortality

The surgical mortality, defined as death within 30 days of surgery, was 2.3% (n=60). The cause of death was postoperative hematomas in 21 cases (35.0 %), tumor progression in 21 (35.0%), infectious diseases in 8 cases (13.3%), postoperative edema and subsequent herniation in 4 cases (6.7%), and other causes in 6 cases (10%) (Table 2). The surgical mortality rate for HGG, LGG, meningiomas and metastases, was 2.9% (n=24), 1.0% (n=3), 0.9% (n=6) and 4.5% (n=20), respectively.

Using multivariate Cox regression analyses, age>60 (Odds ratio (OR) 1.84, 95%CI (1.05, 3.22) , $p<0.05$) and biopsy compared to resection (OR 4.67, 95%CI (1.80, 12.14) $p<0.01$) were shown to be significantly associated with increased surgical mortality (Table 3). Compared to HGG, metastases were associated with a higher mortality in the univariate analysis ($p<0.01$), but this did not reach significance in the multivariate analysis. Compared to HGG, meningiomas were associated with a lower surgical mortality ($p<0.05$).

Postoperative hematomas requiring recraniotomy

The total occurrence of surgically evacuated postoperative hematomas was 2.1% (n=54) (Table 4). Of the 54 evacuated hematomas, 23 (42.6%) were intra-cerebral

(ICH), 13 (24.1%) were acute epidural (EDH), 2 (3.7%) were acute subdural (aSDH), 4 (7.4%) were intracerebellar, 1 (1.9%) was in the brain stem, 8 (14.8%) were chronic subdural hematomas (cSDH), and 3 (5.6%) were subcutaneous (SC) (Table 4).

Risk factors for reoperation for postoperative hematomas

Using multivariate Cox regression analyses, age>60 was shown to be significantly associated with increased risk of developing postoperative hematoma (OR 2.43 95% CI (1.35,4.39), p<0.001) (Table 3). Neither sex, resection vs. biopsy, primary vs. secondary craniotomy, nor tumor type were significantly associated with risk of developing postoperative hematoma. The occurrence of postoperative hematoma was: HGG 2.0% (n=17), LGG 0.7% (n=2), meningiomas 2.3% (n=16), metastases 2.2% (n=10).

Time to reoperation for postoperative hematomas

The surgically evacuated hematomas were reoperated within 6 hours in 11 cases (20.4%), within 12 hours in 14 cases (25.9%), within 24 hours in 21 cases (38.9%), within 48 hours in 35 cases (64.8%), and within 72 hours in 40 cases (74.1%) (Table 4). Four patients were operated between day 3 and day 7 after surgery, 3 patients were operated between day 7 and day 30, and 7 patients after 30 days of surgery. All 7 in the latter group were cSDH. Excluding the cSDHs, the median time from tumor surgery to reoperation for hematoma was 1 day (mean 2.2 days, range 0-26).

Consequences of postoperative hematoma

Twenty patients (37.0 %) had no additional disability, 16 (29.6 %) had minor additional disability, 4 (7.4 %) had major additional disability, and 12 (22.2 %) died due to their hematoma. Long-term data are inconclusive for 2 patients (3.7 %). Six out of twenty-three (26.1 %) patients with ICH died, while 2/13 (15.4 %) patients with EDH died (p>0.05) (Table 4).

Postoperative infection requiring recraniotomy

A total of 39 patients (1.5%) were reoperated for deep postoperative infection (Table 5). Of these infections, 23 (59.0 %) were extradural (ED), 6 (15.4 %) intradural (ID), and 10 (25.6 %) were both intra- and extradural.

Risk factors of reoperation for postoperative infection

Multivariate Cox regression analysis demonstrated that meningiomas had an increased risk of infection compared to gliomas (odds ratio 5.88, 95%CI (2.47,13.87), p<0.001) (Table 3). Men also had an increased risk of infections (p<0.01). Neither resection vs. biopsy, nor primary vs. secondary craniotomy were significantly associated with risk of developing postoperative deep infection. The postoperative infection rate was 1.0% (n=8) for HGG, 0.0% (n=0) for LGG, 3.2% (n=22) for meningiomas, and 1.1% (n=5) for metastases.

Time to reoperation for postoperative infection

The median time from tumor surgery to reoperation for infection was 42 days (mean 95.7 days, range 16-667 days). The number of patients who were reoperated within 1, 2, 3, 6 and 12 months, were 11 (28.2%), 27 (69.2%), 29 (74.4%), 32 (82.1%) and 37 (94.9%), respectively.

Consequences of postoperative infection

Of the 39 patients with deep infection, 29 (74.4 %) had no additional disability, 5 (12.8 %) had minor additional disability, 3 (7.7 %) had major additional disability, 2 (5.1 %) died due to the infection (Table 4).

Discussion

Epidemiology

The neurosurgical catchment area for Oslo University Hospital (OUH) is well-defined, consisting of 2.7 million inhabitants (56% of the Norwegian population) and with very little loss of patients (1%) to other health regions or countries (The Norwegian Cancer Registry, unpublished data). As all patients ≥18 years who underwent craniotomy for an intracranial tumor at OUH within a defined time period of 6 years were included in this study, it can serve as a population study in terms of incidence of craniotomies for particular tumor types in the Norwegian population. The incidence of first-time craniotomy for a brain tumor was 12.8 /100 000 inhabitants per year and for a repeat resection 3.0 /100 000 inhabitants per year.

Surgical mortality at 30 days

The overall surgical mortality in this series was 2.3%. The incidence of surgical mortality after craniotomy for tumors is previously reported to be between 0 and 9.6%, varying with the diagnosis [10, 15, 18-26]. Long et al. [23] reported in 2003 a mortality rate at high-volume hospitals (>50 craniotomies/year) of 2.5% after craniotomy for various intracranial tumors, both benign and malignant. Barker et al. [20] reported in their series of primary supratentorial brain tumors a mortality rate of 2.9%. However, both these studies were in-hospital mortality rates, whereas we report a 30-day mortality rate. Nevertheless, our mortality rates are comparable to, or even lower than, most published rates.

The causes of surgical mortality include complications to surgery and factors not directly related to surgery, as well as other factors, like tumor progression or other morbidity. Several risk factors are associated with increased hazard of death, e.g. advanced age [10, 15, 20, 24], a low preoperative KPS score [15], and comorbidity [10, 20]. Several of the complications are avoidable, and should be paid close attention to.

Postoperative hematomas carry a high mortality rate [17]. In our series, hematomas were suspected to be the cause of, or significant contributor to, 35% of the deaths within 30 days of surgery. Consequently, avoiding hematomas is the single most important factor to reduce surgical mortality.

Pulmonary embolism (PE) has an incidence rate of between 1.5 and 3%, and a mortality rate between 9 and 50%, and is a frequent cause of death among neurosurgical patients [27]. In our study, one patient died from a PE postoperatively. The prevention of PE in neurosurgical patients is controversial, as the commonly used medical prophylaxis, i.e. unfractioned or low-molecular-weight heparin, may increase the rate of intracranial bleeding, with its deleterious effects [28]. Danish et al. showed that mechanical prophylaxis yields outcomes in craniotomy patients superior of those of heparin [28], but the field remains controversial. In our practice, patients with a past hematological history are referred to a consultant hematologist, all patients receive compressive stockings the day before surgery and keep them until fully mobilized. Low-molecular-weight heparin is given the first postoperative day. The patients are mobilized very early, either the same afternoon or on the first postoperative day.

Age is an independent risk factor for surgical mortality. Still, age should not be used as a selection criterion for surgery for intracranial tumors alone [29]. A careful selection among patients with a low preoperative KPS score and with comorbidity should be carried out to lower operative mortality rates.

In our series, undergoing open biopsy was significantly associated with 30-day mortality, a finding that probably has more to do with a selection bias that favors good candidates for resection, while those undergoing biopsy already have a poorer prognosis. A total of 74 patients underwent open biopsy (Table 1). Seven of these patients died within 30 days postoperatively (9.5%), the majority of whom (5 of 7, or 71.4%) died due to tumor progression (Table 2).

In our series, meningiomas had a significantly lower 30-day mortality rate than HGG and metastases, with a rate of 0.9% vs. 2.9% and 4.5%. One factor contributing to this difference might be that all 6 deaths in the meningioma group were surgery-related, while several deaths in the other groups were non-surgery related. However, this factor alone does not explain the discrepancy, indicating that the inherent risk of undergoing a craniotomy will in fact vary according to the diagnosis.

Postoperative hematomas requiring reoperation

In our series, we found a rate of postoperative hematomas of 2.1%. This includes 3 subcutaneous hematomas and 8 cSDH. Other studies have reported a hematoma rate of 0.6-4.0% [15, 18-22, 25, 26, 29, 30].

Risk factors

Advanced age was significantly associated with development of postoperative hematoma, in both uni- and multivariate analyses. This finding is supported by other studies [13, 17, 31] and has been attributed to tissue fragility observed in the elderly [28]. Palmer et al. [17] showed in their series of 6668 intracranial procedures an increased risk of postoperative hematoma for meningiomas compared with intrinsic tumors. We did not find an association between histology and risk of postoperative hematoma.

In the aforementioned series, Palmer et al. [17] identified several risk factors associated with postoperative hematoma, including thrombocytopenia, anticoagulants, a history of heavy alcohol intake, coagulopathy, malignancy outside the central nervous system, and the administration of antiplatelet agents during the 2 weeks preceding surgery. Administration of antiplatelet agents was the most frequent risk factor, being used by 43% of those reoperated for hematoma [17]. In our practice, patients with a past hematological history are referred to a consultant hematologist, aspirin is stopped at least 10 days prior to surgery and when on anticoagulation, the INR should be below 1.5. Low-molecular-weight heparin is not given until the first postoperative day.

Mortality rate of postoperative hematomas

The reported mortality rate of postoperative hematomas is 18-32% [17, 32, 33]. We found a mortality rate of 22%, with an additional 2% being severely disabled due to the hematoma. Consequently, postoperative hematomas may have deleterious consequences and it is utmost important to reduce or eliminate as many risk factors as possible, and thereby reducing the incidence of postoperative hematomas. Vassilouthis et al. [34] indicated in their series of 526 patients undergoing craniotomy, that the incidence of postoperative intracranial hematoma should become negligible, provided that necessary modifications regarding anesthesia are adopted. Their strict anesthesiological protocol included a deep opioid analgesia to eliminate any acute

elevations of the arterial pressure during and immediately after craniotomy. Furthermore, emergence from anaesthesia was delayed for an average of 1 1/2-2 h following the neurosurgical procedure. Even though postoperative hematomas occur rarely, more studies on how to avoid them are needed, as the consequences of them are often devastating.

Timing of postoperative intracranial hematoma development

Taylor et al. [32] reported a 2.2% rate of postoperative hematomas in their series of 2305 patients undergoing intracranial surgery of miscellaneous reasons. Clinical deterioration as a result of postoperative hematoma occurred within 6 hours of surgery in 88% of the cases and <24 hours after surgery in the remaining 12% hematoma cases. They concluded that a 6-hour observation period in the recovery area/intensive care unit after craniotomy before transfer to further nursing on a neurosurgical ward should be sufficient for most patients, but they recommended longer observation times after emergency craniotomies and posterior fossa surgery. In our series, only 11 patients (25%) were reoperated within 6 hours, indicating that a 6-hour observation period in recovery may be insufficient to sift out the majority of the patients in need of emergency surgery for a postoperative hematoma. However, close observation on a specialized neurosurgical ward may overcome this problem. Furthermore, our results indicate that a patient undergoing a craniotomy should be observed closely for a total of at least 48 hours postoperatively, as 80% of our patients that needed a recraniotomy for postoperative hematoma are operated within 2 days.

Postoperative infections requiring reoperation

Contemporary neurosurgical series have reported an incidence of postoperative infections after craniotomy of 0.6-6.6% [18, 19, 30, 35-37], although some of these series have included non-operative cases as well. Our rate of postoperative infections requiring surgical treatment was in this study 1.5%, thus being in the lower end of the scale.

Risk factors

We observed a statistically significant association between male gender and postoperative infections. This has not been noted in other large neurosurgical series

[38-40], but Korinek et al. [41] observed an increased risk of nosocomial meningitis after craniotomy in males. At present, we have no explanation for our finding.

Meningioma surgery was significantly associated with development of postoperative infection in both uni- and multivariate analyses. This was also shown by Korinek et al. [35] in 2005, although only in univariate analysis. They attributed this to hemostasis and closure difficulties in meningioma surgery. Korinek et al. [35] also showed an association between infection and surgery duration over 4 hours, a finding that also has been demonstrated by others [42, 43]. As meningioma operations are often time -consuming procedures, this might be a contributing factor to the higher incidence of infections after meningioma surgery.

Korinek et al. [35] studied the effect of antibiotic prophylaxis (ABP) on neurosurgical site infections after craniotomy for various reasons, e.g. tumor surgery, vascular surgery, and trauma surgery. Among the 4578 patients studied, 77 (1.7%) developed bone flap osteitis, and 126 (2.7%) developed brain abscess or subdural empyema, for a total of 4.4%. As patients with both osteitis and abscess/empyema were counted once in each group, the number of patients with infections was a bit lower. ABP significantly reduced the incidence of bone flap osteitis (3.1% in patients with no ABP and 1.3% in patients with ABP, $p<0.0002$) and abscess/empyema (5.6% versus 2.0%, $p<0.0001$). In our practice, we use a second-generation cephalosporin i.v. at initiation of surgery and continued every 90 minutes until the case is completed or the maximum daily dose of 8 grams is reached, whereafter erythromycin or a third-generation cephalosporin is started and continued until completion of the case.

Consequences of postoperative infection

The consequences of postoperative infection are not at all as severe as the consequences of postoperative hematoma. In our series, 2 patients (5%) died due to the infection, while 33 (85%) had a good outcome, with no or only a mild disability (Table 2). It is important to point out that we did not include patients with meningitis.

Timing of postoperative infection development

In our series, almost 75% of the patients with infection were reoperated within 3 months of tumor surgery. Korinek et al. [35] showed a mean time between surgery and

onset of infection of 118±157 days for bone flap osteitis, and 25±27 days for brain abscesses or subdural empyema. Dashti et al. [36] reported a median duration between craniotomy and presentation of postoperative infection of 1.5 months (range 4 days-5 years). In our series, most postoperative infections requiring reoperation occur within 3 months of surgery, but some infections, in particular bone flap osteitis, may occur later than 1 year after surgery, reportedly as late as 5 years later [43, 44].

Strengths of the study

The strengths of this study lie in the setting, design and follow-up. The data were restricted to one health centre only (Oslo University Hospital), thereby reducing the possible confounding effect of differences in the access to health care services between health centers. Thus, we have avoided the selection bias inherently present in large multi-center studies, as there are only two neurosurgical units performing these surgeries in a geographically well-defined area. As Dashti et al. [36] pointed out, it is reasonable to assume that a number of patients with postoperative infection were not included in their study if they presented to, and were subsequently treated at, other facilities than the one where they were operated in the first place. They also point out that this number might be high, but that there is no way to determine how high [36]. This problem may have occurred in several of the other studies as well. Furthermore, our data were prospectively registered in a database. As the study includes all craniotomies performed for a histologically verifiable brain tumor, there is no selection bias. The study is contemporary, thereby reflecting current neurosurgical practice and was performed within a relatively short time span, thereby reducing confounding factors as changes in antibiotic prophylaxis regimen or operating theatres. With respect to data, we only used end points that are easily verifiable (mortality, reoperation for hematomas, reoperations for infections). Lastly, we obtained 100% follow-up. To the best of our knowledge, our study is the largest study with regard to postoperative complications within 30 days of craniotomy for brain tumors. Previous studies are either smaller than our study, or they use in-hospital mortality rates.

Limitations of the study

The first limitation of the study is the retrospective design. Secondly, the follow-up on some patients may be too short with regard to postoperative infections, as bone flap infections may occur later than 1 year after surgery.

Conclusions

The annual incidence of first-time craniotomy for a brain tumor was 12.8 /100 000 inhabitants. The mortality rate, rate of postoperative hematomas and infections were low. Although advanced age was significantly associated with a higher 30-day surgical mortality and risk of postoperative hematomas, surgery in selected elderly patients is worthwhile and not futile. The single most important way to reduce surgical mortality is avoidance of postoperative hematomas.

References

1. CTBRUS. Statistical Report: Primary Brain Tumors in the United States, 2000–2004.*http://www.cbtrus.org/reports//2007-2008/2007report.pdf.* 2008.

2. Percy AK, Elveback LR, Okazaki H, Kurland LT. Neoplasms of the central nervous system. Epidemiologic considerations. *Neurology.* Jan 1972;22(1):40-48.

3. Claus EB, Horlacher A, Hsu L, et al. Survival rates in patients with low-grade glioma after intraoperative magnetic resonance image guidance. *Cancer.* Mar 15 2005;103(6):1227-1233.

4. McGirt MJ, Chaichana KL, Gathinji M, et al. Independent association of extent of resection with survival in patients with malignant brain astrocytoma. *J Neurosurg.* Jan 2009;110(1):156-162.

5. Keles GE, Chang EF, Lamborn KR, et al. Volumetric extent of resection and residual contrast enhancement on initial surgery as predictors of outcome in adult patients with hemispheric anaplastic astrocytoma. *J Neurosurg.* Jul 2006;105(1):34-40.

6. Mirimanoff RO, Dosoretz DE, Linggood RM, Ojemann RG, Martuza RL. Meningioma: analysis of recurrence and progression following neurosurgical resection. *J Neurosurg.* Jan 1985;62(1):18-24.

7. Hart MG, Grant R, Walker M, Dickinson H. Surgical resection and whole brain radiation therapy versus whole brain radiation therapy alone for single brain metastases. *Cochrane Database Syst Rev.* 2005(1):CD003292.

8. Vecht CJ, Avezaat CJ, van Putten WL, Eijkenboom WM, Stefanko SZ. The influence of the extent of surgery on the neurological function and survival in malignant glioma. A retrospective analysis in 243 patients. *J Neurol Neurosurg Psychiatry.* Jun 1990;53(6):466-471.

9. Nitta T, Sato K. Prognostic implications of the extent of surgical resection in patients with intracranial malignant gliomas. *Cancer.* Jun 1 1995;75(11):2727-2731.

10. Barker FG, 2nd. Craniotomy for the resection of metastatic brain tumors in the U.S., 1988-2000: decreasing mortality and the effect of provider caseload. *Cancer.* Mar 1 2004;100(5):999-1007.

11. Fadul C, Wood J, Thaler H, Galicich J, Patterson RH, Jr., Posner JB. Morbidity and mortality of craniotomy for excision of supratentorial gliomas. *Neurology.* Sep 1988;38(9):1374-1379.

12. Kalfas IH, Little JR. Postoperative hemorrhage: a survey of 4992 intracranial procedures. *Neurosurgery.* Sep 1988;23(3):343-347.

13. Gerlach R, Raabe A, Scharrer I, Meixensberger J, Seifert V. Post-operative hematoma after surgery for intracranial meningiomas: causes, avoidable risk factors and clinical outcome. *Neurol Res.* Jan 2004;26(1):61-66.

14. Mahaley MS, Jr., Mettlin C, Natarajan N, Laws ER, Jr., Peace BB. National survey of patterns of care for brain-tumor patients. *J Neurosurg.* Dec 1989;71(6):826-836.

15. Sawaya R, Hammoud M, Schoppa D, et al. Neurosurgical outcomes in a modern series of 400 craniotomies for treatment of parenchymal tumors. *Neurosurgery.* May 1998;42(5):1044-1055.

16. Paek SH, Audu PB, Sperling MR, Cho J, Andrews DW. Reevaluation of surgery for the treatment of brain metastases: review of 208 patients with single or multiple brain metastases treated at one institution with modern neurosurgical techniques. *Neurosurgery.* May 2005;56(5):1021-1034; discussion 1021-1034.

17. Palmer JD, Sparrow OC, Iannotti F. Postoperative hematoma: a 5-year survey and identification of avoidable risk factors. *Neurosurgery.* Dec 1994;35(6):1061-1064.

18. Morokoff AP, Zauberman J, Black PM. Surgery for convexity meningiomas. *Neurosurgery.* Sep 2008;63(3):427-433.

19. Chang SM, Parney IF, McDermott M, et al. Perioperative complications and neurological outcomes of first and second craniotomies among patients enrolled in the Glioma Outcome Project. *J Neurosurg.* Jun 2003;98(6):1175-1181.

20. Barker FG, 2nd, Curry WT, Jr., Carter BS. Surgery for primary supratentorial brain tumors in the United States, 1988 to 2000: the effect of provider caseload and centralization of care. *Neuro Oncol.* Jan 2005;7(1):49-63.

21. Curry WT, McDermott MW, Carter BS, Barker FG, 2nd. Craniotomy for meningioma in the United States between 1988 and 2000: decreasing rate of mortality and the effect of provider caseload. *J Neurosurg.* Jun 2005;102(6):977-986.

22. Boviatsis EJ, Bouras TI, Kouyialis AT, Themistocleous MS, Sakas DE. Impact of age on complications and outcome in meningioma surgery. *Surg Neurol.* Oct 2007;68(4):407-411.

23. Long DM, Gordon T, Bowman H, et al. Outcome and cost of craniotomy performed to treat tumors in regional academic referral centers. *Neurosurgery.* May 2003;52(5):1056-1063.

24. Cowan JA, Jr., Dimick JB, Leveque JC, Thompson BG, Upchurch GR, Jr., Hoff JT. The impact of provider volume on mortality after intracranial tumor resection. *Neurosurgery.* Jan 2003;52(1):48-53.

25. Stark AM, Tscheslog H, Buhl R, Held-Feindt J, Mehdorn HM. Surgical treatment for brain metastases: prognostic factors and survival in 177 patients. *Neurosurg Rev.* Apr 2005;28(2):115-119.

26. Brell M, Ibanez J, Caral L, Ferrer E. Factors influencing surgical complications of intraaxial brain tumours. *Acta Neurochir (Wien).* 2000;142(7):739-750.

27. Danish SF, Burnett MG, Stein SC. Prophylaxis for deep venous thrombosis in patients with craniotomies: a review. *Neurosurg Focus.* Oct 15 2004;17(4):E2.

28. Danish SF, Burnett MG, Ong JG, Sonnad SS, Maloney-Wilensky E, Stein SC. Prophylaxis for deep venous thrombosis in craniotomy patients: a decision analysis. *Neurosurgery.* Jun 2005;56(6):1286-1292; discussion 1292-1284.

29. Rogne SG, Konglund A, Meling TR, et al. Intracranial tumor surgery in patients >70 years of age: is clinical practice worthwhile or futile? *Acta Neurol Scand.* Sep 8 2009.

30. Rabadan AT, Hernandez D, Eleta M, et al. Factors related to surgical complications and their impact on the functional status in 236 open surgeries for malignant tumors in a Latino-American hospital. *Surg Neurol.* Oct 2007;68(4):412-420; discussion 420.

31. Boviatsis EJ, Bouras TI, Kouyialis AT, Themistocleous MS, Sakas DE. Impact of age on complications and outcome in meningioma surgery. *Surg Neurol.* Oct 2007;68(4):407-411; discussion 411.

32. Taylor WA, Thomas NW, Wellings JA, Bell BA. Timing of postoperative intracranial hematoma development and implications for the best use of neurosurgical intensive care. *J Neurosurg.* Jan 1995;82(1):48-50.

33. Basali A, Mascha EJ, Kalfas I, Schubert A. Relation between perioperative hypertension and intracranial hemorrhage after craniotomy. *Anesthesiology.* Jul 2000;93(1):48-54.

34. Vassilouthis J, Anagnostaras S, Papandreou A, Dourdounas E. Is postoperative haematoma an avoidable complication of intracranial surgery? *Br J Neurosurg.* Apr 1999;13(2):154-157.

35. Korinek AM, Golmard JL, Elcheick A, et al. Risk factors for neurosurgical site infections after craniotomy: a critical reappraisal of antibiotic prophylaxis on 4,578 patients. *Br J Neurosurg.* Apr 2005;19(2):155-162.

36. Dashti SR, Baharvahdat H, Spetzler RF, et al. Operative intracranial infection following craniotomy. *Neurosurg Focus.* 2008;24(6):E10.

37. McClelland S, 3rd, Hall WA. Postoperative central nervous system infection: incidence and associated factors in 2111 neurosurgical procedures. *Clin Infect Dis.* Jul 1 2007;45(1):55-59.

38. Mollman HD, Haines SJ. Risk factors for postoperative neurosurgical wound infection. A case-control study. *J Neurosurg.* Jun 1986;64(6):902-906.

39. Lietard C, Thebaud V, Besson G, Lejeune B. Risk factors for neurosurgical site infections: an 18-month prospective survey. *J Neurosurg.* Oct 2008;109(4):729-734.

40. Korinek AM. Risk factors for neurosurgical site infections after craniotomy: a prospective multicenter study of 2944 patients. The French Study Group of Neurosurgical Infections, the SEHP, and the C-CLIN Paris-Nord. Service Epidemiologie Hygiene et Prevention. *Neurosurgery.* Nov 1997;41(5):1073-1079.

41. Korinek AM, Baugnon T, Golmard JL, van Effenterre R, Coriat P, Puybasset L. Risk factors for adult nosocomial meningitis after craniotomy: role of antibiotic prophylaxis. *Neurosurgery.* Jul 2006;59(1):126-133.

42. Idali B, Lahyat B, Khaleq K, Ibahioin K, El Azhari A, Barrou L. [Postoperative infection following craniotomy in adults]. *Med Mal Infect.* May 2004;34(5):221-224.

43. Korinek AM. Risk factors for neurosurgical site infections after craniotomy: a prospective multicenter study of 2944 patients. The French Study Group of Neurosurgical Infections, the SEHP, and the C-CLIN Paris-Nord. Service Epidemiologie Hygiene et Prevention. *Neurosurgery.* Nov 1997;41(5):1073-1079; discussion 1079-1081.

44. Blomstedt GC. Infections in neurosurgery: a retrospective study of 1143 patients and 1517 operations. *Acta Neurochir (Wien).* 1985;78(3-4):81-90.

Financial Disclosure

A research grant to the project was given by Schering-Plough (4000 Euro).

Acknowledgement

We thank Elisabeth Elgesem and Hanne Vebenstad for excellent secretarial assistance.

List of legends

Table 1: Patient characteristics

	N	%
Patients	2630	100
Department		
Rikshospitalet	1693	64.4
Ullevål	937	35.6
Sex		
Male	1275	48.5
Female	1355	51.5
Age (years)		
18 –29.9	141	5.4
30 - 39.9	300	11.4
40 –49.9	437	16.6
50 – 59.9	604	23.0
60 – 69.9	649	24.7
70 – 79.9	411	15.6
>80	88	3.3
Type of surgery		
Primary	2141	81.4
Second	489	18.6
Craniotomy		
Resection	2556	97.2
Open biopsy	74	2.8
Main histology		
High-grade glioma (HGG)	830	31.6
Meningioma	693	26.3
Metastases	449	17.1
Low-grade glioma (LGG)	289	11.0
Schwannoma	73	2.8
Primary CNS-lymphoma	51	1.9
CNS hemangioblastoma	39	1.5
Cavernous hemangioma	38	1.4
Pituitary adenoma	8	0.3
Others	160	6.1

Table 2: Patients who died within 30 days of tumor surgery (surgical mortality cases) (n=60)

Age	Sex	Histology*	Op.type**	Time***	Comments
43	M	Hemangioblastoma	R	3	Postop. hematoma
29	F	HGG	R	17	Tumor progression
41	M	HGG	R	13	Postop. brain edema/herniation
41	F	HGG	R	3	Postop. hematoma
48	M	HGG	B	10	Pneumonia
49	F	HGG	R	11	Tumor progression
54	F	HGG	R	2	Tumor progression
56	F	HGG	B	8	Postop. hematoma
60	M	HGG	R	30	Postop. hematoma
64	M	HGG	R	17	Tumor progression
64	F	HGG	R	4	Postop. brain edema/herniation
65	F	HGG	R	22	Postop. hematoma
66	F	HGG	R	24	Tumor progression
67	F	HGG	R	5	Tumor progression
67	M	HGG	R	19	Tumor progression
69	M	HGG	B	29	Tumor progression
74	F	HGG	R	30	Tumor progression
75	M	HGG	R	11	Postop. hematoma
75	M	HGG	R	22	Tumor progression
76	M	HGG	R	15	Postop. hematoma
76	F	HGG	R	4	Postop. hematoma
77	F	HGG	R	8	Postop. hematoma
81	F	HGG	B	28	Tumor progression
82	M	HGG	R	21	Pulmonary embolism
84	F	HGG	R	14	Postop. brain edema/herniation
32	F	LGG	R	17	Shunt failure
48	M	LGG	R	18	Pneumonia
68	M	LGG	R	24	Postop. hematoma
62	M	Lymphoma	B	12	Tumor progression
75	F	Lymphoma	B	13	Tumor progression
78	M	Lymphoma	B	26	Tumor progression
31	F	Melanocytoma	R	11	Tumor progression
55	F	Meningioma	R	6	Postop. brain edema/herniation
73	M	Meningioma	R	11	Postop. hematoma
77	M	Meningioma	R	4	Postop. hematoma
79	F	Meningioma	R	12	Postop. hematoma
83	M	Meningioma	R	15	Pneumonia
83	M	Meningioma	R	29	Cardiac arrest
35	M	Metastasis	R	12	Tumor progression
40	M	Metastasis	R	27	Pneumonia
45	F	Metastasis	R	4	Postop. hematoma
46	F	Metastasis	R	9	Hydrocephalus
49	F	Metastasis	R	25	Postop. hematoma
49	F	Metastasis	R	26	Postop. hematoma
52	M	Metastasis	R	6	Postop. hematoma
53	F	Metastasis	R	5	Tumor progression
56	M	Metastasis	R	3	Cardiac arrest
60	M	Metastasis	R	1	Postop. hematoma
61	M	Metastasis	R	30	Postop. hematoma
61	F	Metastasis	R	12	Pneumonia

62	M	Metastasis	R	19	Tumor progression
62	M	Metastasis	R	29	Postop. hematoma
65	F	Metastasis	R	22	Sepsis
71	F	Metastasis	R	25	Tumor progression
73	M	Metastasis	R	24	Sepsis
77	F	Metastasis	R	19	Tumor progression
78	M	Metastasis	R	29	Subdural empyema
81	F	Metastasis	R	25	Tumor progression
48	M	Pituitary adenoma	R	16	Cerebral infarction
69	M	Pituitary adenoma	R	9	Postop. hematoma

Abbreviations:

M = male, F = female

*Histology: HGG = high-grade glioma, LGG = low-grade glioma

**Op. type = Resection (R) or biopsy (B)

***Time = Time to death in days after primary surgery

Table 3. Univariate and multivariate analysis of factors possibly associated with surgical mortality, surgery for postoperative infection and surgery for postoperative hematoma

	30 day mortality		Infection		Postop hematoma	
	Univariate Odds Ratio (95% CI)	Multivariate Odds Ratio (95% CI)	Univariate Odds Ratio (95% CI)	Multivariate Odds Ratio (95% CI)	Univariate Odds Ratio (95% CI)	Multivariate Odds Ratio (95% CI)
Age >60 *No/Yes*	2.27** [1.34,3.86]	1.84* [1.05,3.22]	1.11 [0.59,2.09]	0.97 [0.50,1.86]	2.42** [1.38,4.26]	2.43** [1.35,4.39]
Sex *Male/Female*	0.94 [0.56,1.57]	1.09 [0.64,1.84]	0.47* [0.24,0.91]	0.33** [0.16,0.66]	0.94 [0.55,1.61]	0.94 [0.54,1.64]
Primary Op *Primary/secondary*	0.77 [0.38,1.57]	1.01 [0.48,2.13]	1.74 [0.86,3.51]	2.01 [0.97,4.17]	0.99 [0.50,1.99]	1.14 [0.56,2.31]
Operation *Resection/Biopsy*	4.93*** [2.16,11.26]	4.67** [1.80,12.14]	a)	a)	a)	a)
Histology						
HGG	1	1	1	1	1	1
LGG	0.53 [0.16,1.69]	0.44 [0.13,1.53]	a)	a)	0.38 [0.09,1.58]	0.59 [0.13,2.66]
Meningioma	0.30** [0.13,0.71]	0.30* [0.12,0.76]	3.70*** [1.95,7.02]	4.61*** [1.98,10.73]	1.18 [0.65,2.13]	1.08 [0.53,2.19]
Metastasis	2.50** [1.44,4.31]	1.51 [0.81,2.80]	0.71 [0.28,1.83]	1.34 [0.43,4.21]	1.11 [0.55,2.22]	0.95 [0.43,2.10]
Lymphoma	2.77 [0.84,9.14]	0.91 [0.23,3.64]	1.34 [0.18,9.94]	3.43 [0.41,28.80]	a)	a)
Capillary hemangioblastoma	1.13 [0.15,8.37]	1.01 [0.13,7.72]	a)	a)	2.64 [0.62,11.24]	2.67 [0.59,12.12]
Schwannoma	0.42 [0.13,1.34]	0.40 [0.12,1.34]	0.43 [0.10,1.79]	0.75 [0.16,3.56]	1.00 [0.42,2.36]	1.21 [0.47,3.15]
Others	0.42 [0.13,1.34]	0.40 [0.12,1.36]	0.92 [0.12,6.80]	1.61 [0.20,13.19]	0.66 [0.09,4.81]	0.76 [0.10,5.84]
Observations		2557		2286		2523
Pseudo-R^2		0,064		0,069		0,025
H-L test		p =0.66		p=0.85		P=0.78

HGG=High grade glioma

LGG=Low grade glioma

H-L= Hosmer-Lemeshow

a) Insufficient events in one of the contrasting categories to calculate odds ratio

Table 4. Patients reoperated for postoperative hematoma (n=54)

Age	Sex	Histology*	Location**	Time to reop (hh:mm)***	Outcome****	Time to death (days)*****
63	F	Carcinoma	SC	19:45	NAD	
65	M	Carcinoma	EDH	69:53	Minor	
43	M	Hemangioblastoma	Brain stem	28:35	Death	3
77	M	Hemangioblastoma	Cerebellum	47:04	NAD	
31	M	HGG	ICH	14:15	NAD	
33	M	HGG	cSDH	107 days	NAD	
34	M	HGG	Cerebellum	152:57	Minor	
46	F	HGG	EDH	26:22	NAD	
48	F	HGG	ICH	01:36	Minor	
55	F	HGG	ICH	06:20	Minor	
57	M	HGG	cSDH	43 days	NAD	
58	M	HGG	ICH	44:10	NA	
65	F	HGG	ICH	16:58	Death	22
70	F	HGG	EDH	74:25	NAD	
72	F	HGG	EDH	02:50	Minor	
75	M	HGG	ICH	01:35	Death	11
76	M	HGG	SC	03:15	NAD	
76	F	HGG	ICH	30:38	Minor	
76	F	HGG	ICH	04:12	Death	4
77	F	HGG	EDH	07:57	Death	8
81	M	HGG	EDH	30:17	Minor	
51	M	LGG	EDH	46:06	Minor	
60	F	LGG	ICH	27:35	NAD	
52	M	Melanocytoma	EDH	42:45	NAD	
51	M	Meningioma	EDH	48:50	NAD	
52	F	Meningioma	aSDH	10 days	NAD	
54	F	Meningioma	ICH	93:35	Major	
60	F	Meningioma	ICH	02:20	Minor	
67	F	Meningioma	ICH	14:20	Minor	
69	F	Meningioma	ICH	01:45	NAD	
69	F	Meningioma	cSDH	47 days	NAD	
69	F	Meningioma	ICH	22:00	Minor	
70	M	Meningioma	SC	06:20	NAD	
70	M	Meningioma	cSDH	73 days	NAD	
71	F	Meningioma	Cerebellum	22:20	Major	
75	F	Meningioma	ICH	167:45	NA	
76	M	Meningioma	ICH	03:27	Major	
78	M	Meningioma	ICH	03:40	Minor	
78	F	Meningioma	cSDH	383 days	Death	390
80	F	Meningioma	cSDH	13 days	Minor	
45	F	Metastasis	ICH	45:20	Death	4
49	F	Metastasis	ICH	26 days	Death	26
52	M	Metastasis	EDH	17:41	Death	6
54	M	Metastasis	EDH	53:07	NAD	
61	M	Metastasis	Cerebellum	38:05	Death	30
63	F	Metastasis	ICH	32:40	Minor	
68	M	Metastasis	ICH	03:40	Minor	
72	F	Metastasis	EDH	04:15	NAD	
73	F	Metastasis	cSDH	68 days	NAD	

73	M	Metastasis	ICH	47:17	Death	54
62	M	Pituitary adenoma	ICH	58:10	Major	
69	M	Pituitary adenoma	aSDH	45:15	Death	9
69	M	Pituitary adenoma	cSDH	107 days	Minor	
46	M	Schwannoma	EDH	61:08	NAD	

Abbreviations:

M = male, F = female

*Histology: HGG = high-grade glioma, LGG = low-grade glioma

**Location of hematoma: SC = subcutaneous hematoma, EDH = epidural hematoma, aSDH = acute subdural hematoma, cSDH = chronic subdural hematoma, ICH = intracerebral hematoma

***Time = time of reoperation in hours and minutes after primary surgery

****Outcome = hematoma-inflicted disability: NAD = no additional disability, Minor = minor additional disability, Major = major additional disability, NA = no information available

*****Time to death = time from tumor surgery to death, when caused by the hematoma

Table 5. Patients reoperated for postoperative infections (n=39)

Age	Sex	Histology*	Location**	Time to reop. (days)***	Outcome****
18	M	HGG	ED	16	NAD
40	M	HGG	ED	46	NAD
57	M	HGG	ED	20	NAD
59	M	HGG	ED	307	NAD
64	M	HGG	ED	49	Death
69	M	HGG	ED	80	Major
70	M	HGG	ED	20	NAD
70	F	HGG	ID	25	NAD
34	M	Lymfoma	ED	667	NAD
26	F	Meningioma	ED	71	NAD
33	F	Meningioma	ED	119	NAD
38	M	Meningioma	ED	248	NAD
40	F	Meningioma	ED	270	NAD
42	F	Meningioma	ED/ID	25	Minor
49	M	Meningioma	ED/ID	29	NAD
51	M	Meningioma	ID	31	NAD
53	F	Meningioma	ED	42	NAD
55	M	Meningioma	ED	18	NAD
56	M	Meningioma	ID	45	NAD
56	F	Meningioma	ED/ID	38	Minor
56	M	Meningioma	ED	35	NAD
58	M	Meningioma	ED	59	NAD
64	M	Meningioma	ID	59	NAD
66	M	Meningioma	ED/ID	40	NAD
71	M	Meningioma	ED/ID	37	NAD
72	M	Meningioma	ED	37	NAD
74	F	Meningioma	ED	190	Minor
74	M	Meningioma	ID	36	NA
75	M	Meningioma	ED/ID	38	NAD
76	M	Meningioma	ED/ID	56	NAD
78	F	Meningioma	ED	17	Minor
45	M	Metastasis	ED/ID	25	NAD
59	F	Metastasis	ED/ID	116	Minor
63	M	Metastasis	ED	25	NAD
71	M	Metastasis	ED/ID	109	Major
78	M	Metastasis	ID	20	Death
66	F	Other (MFH)	ED	393	NAD
62	M	Pituitary adenoma	ED	232	Major
40	F	Schwannoma	ED	43	NAD

Abbreviations:

M = male, F = female

*Histology: HGG = high-grade glioma, LGG = low-grade glioma

**Location = location of infection: ED = extradural infection, ID = intradural infection, ED/ID = both intradural and extradural infection

***Time = time of reoperation in days after primary surgery

****Outcome = clinical outcome after postoperative infection: NAD = no additional disability, Minor = minor additional disability, Major = major additional disability.